Psychotic-like symptoms and positive schizotypy are associated with mixed and ambiguous handedness in an adolescent community sample.

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Abstract:

The objective of this study was to replicate the association between atypical handedness and psychosis-proneness in a representative sample of adolescents from the general population. It expands previous studies by (1) analyzing a variety of atypical handedness indexes (left, mixed, ambiguous, and inconsistent), (2) measuring comprehensively the multidimensionality of psychosis-proneness, and (3) analyzing the association of different patterns of atypical handedness with nonclinical dimensions of both trait (schizotypy) and sub-clinical symptom (psychotic-like experiences) levels. Seven hundred and twenty-eight adolescents were assessed for handedness by the 12-item self-report Annett Hand Preference Questionnaire and for psychosis-proneness by the Oxford-Liverpool Inventory of Feelings and Experiences and the Community Assessment of Psychic Experiences scales. Writing-hand alone did not detect associations between laterality and psychosis-proneness. Mixed- rather than left-handedness was related to psychosis-proneness, and this was more evident when analyzing subjects with ambiguous handedness exclusively. When analysis was restricted to subjects with non-ambiguous handedness, strong left-handedness was related to psychosis-proneness. The positive dimension showed a stronger association than the negative one with atypical handedness. Results partially support mixed-handedness as a marker of developmental disorders underlying both atypical lateralization and psychosis-proneness. Among various possible mixed-handedness patterns, inconsistent hand use across primary actions, and for the same action across time, seems particularly related to psychosis-proneness and thus requires further exploration.

Keywords: psychosis-proneness | schizophrenia | laterality | atypical handedness | adolescents | pyschology

Article:

1. Introduction

Schizotypy phenotypes in the general population share etiopathogenic mechanisms and risk factors with schizophrenia, supporting the notion of psychosis as a continuum ranging from nonclinical to clinical deviance (van Os et al., 2009). The nonclinical psychosis phenotype (i.e., psychosis-proneness) is observed and reliably measured at the level of schizotypic personality features (using trait-like measures) and psychotic-like experiences (using symptom-based measures; Kwapil et al., 1999, Stefanis et al., 2002, Barrantes-Vidal et al., 2009 and Barrantes-Vidal et al., 2010). A substantial body of work has demonstrated that psychometrically assessed schizotypy is associated cross-sectionally with laboratory, interview, cognitive, and biobehavioral measures of schizophrenic symptoms and impairment (Claridge, 1997; Raine, 2006; Blanchard et al., 2011; Kwapil et al., 2012). Furthermore, longitudinal research indicates that psychometric schizotypy is associated with the development of psychosis and schizophrenia-spectrum disorders (e.g., Chapman et al., 1994; Gooding et al., 2005) with effect sizes as large as or larger than in studies of consanguinity. The study of psychosis-proneness in nonclinical samples allows the analysis of risk factors without the confounding effects of psychosis (e.g., medication, symptom severity, and stigma).

An abnormality in cerebral lateralization has long been related to the etiology of schizophrenia (Crow, 1990 and Sommer et al., 2001) and more recently of schizotypy (Richardson et al., 1997 and Somers et al., 2009). This fits well with the view that schizophrenia is a neurodevelopmental disorder that originates at the time when brain asymmetries are being established (Lewis and Murray, 1987 and Weinberger, 1996). Handedness is a simple way of capturing atypical lateralization—although there are a variety of hand preference patterns. Thus, the conceptualization and measurement of atypical handedness is a complex issue. Mixed handedness refers to using different hands for different actions (across-items inconsistency) (Claridge et al., 1998 and Schürhoff et al., 2008), whereas ambiguous handedness refers to the use of different hands for the same action across time (within-item inconsistency; Hayden et al., 1997). However, some authors (e.g., Shaw et al., 2001 and Chapman et al., 2011) had participants self-report rather than demonstrate handedness, referring to ambiguous handedness as the report of using “either hand” for an action. However, studies have not comprehensively examined the relation of psychosis-proneness with hand preference patterns, including inconsistency across both items and time.

There is consistent evidence of mixed handedness in schizophrenic patients (Dragovic and Hammond, 2005 and Dragovic et al., 2005). Similarly, several studies in nonclinical subjects have found that psychosis-proneness is associated with mixed handedness (Chapman and

Chapman, 1987, Kim et al., 1992, Poreh, 1994, Richardson, 1994, Claridge et al., 1998, Shaw et al., 2001, Gregory et al., 2003, Dragovic et al., 2005, Annett and Moran, 2006, Schürhoff et al., 2008 and Chapman et al., 2011), although some studies have found associations with both left and mixed handedness (Kelley and Coursey, 1992 and Poreh et al., 1997).

Most of these studies focused on the association of atypical handedness with positive schizotypy, which features cognitive-perceptual distortions of this multidimensional construct (Kwapil et al., 2008). Disorganized features have also been related to atypical handedness in nonclinical samples (Kim et al., 1992, Stefanis et al., 2006 and Schürhoff et al., 2008); however, most studies show a preferential focus on the positive dimension scales. Some studies suggested that mixed handedness and negative schizotypy are minimally related (Chapman and Chapman, 1987 and Stefanis et al., 2006), although less strongly than with positive traits (Kim et al., 1992 and Chapman et al., 2011). However, other indicators of developmental instability, such as dermatoglyphic asymmetry and minor physical anomalies, tend to be associated with negative schizotypy (Rosa et al., 2000, Barrantes-Vidal et al., 2003 and Blanchard et al., 2010). As atypical handedness is considered a marker of neurodevelopmental disturbance (Reilly et al., 2001), it would be useful to clarify its relation with negative schizotypy.

The present study aimed to replicate the association between atypical handedness and psychosis-proneness in a representative sample of adolescents from the general population. We expanded upon previous studies by (1) including multiple handedness indexes, (2) comprehensively measuring the multidimensionality of psychosis-proneness (positive, disorganized and negative dimensions), and (3) analyzing the association of different patterns of atypical handedness with nonclinical dimensions of both trait (schizotypy) and sub-clinical symptom (psychotic-like experiences) levels. Additionally, we addressed this topic in adolescence—a group for whom this topic is relatively understudied. Note that both handedness (Fonseca-Pedrero et al., 2007) and psychosis-proneness (Barrantes-Vidal et al., 2003 and Fonseca-Pedrero et al., 2010) can be reliably assessed in adolescents.

2. Method

2.1. Subjects

Participants were community adolescents in secondary obligatory education randomly selected from the School Census of Barcelona. The study was approved by the Ethical Committee of the Universitat Autònoma de Barcelona and by the corresponding School Board. Additionally, parental consent and participant assent were obtained prior to participation. From the initial

sample (n=927), 95 students who were non-native Spanish speakers students were excluded due to limited command of the language. Another 99 students with elevated scores on the Eysenck Personality Questionnaire (Eysenck and Eysenck, 1975) Lie scale and five who did not complete the questionnaires were excluded. The final sample consisted of 728 subjects evenly distributed by sex (Time 1 sample). Mean age was 14.3 (S.D.=0.6) and was not significantly different for females (mean=14.4, S.D.=0.6) and males (mean=14.5, S.D.=0.6) ($t(720)=-1.51$).

An average of 7 months later, a subsample was recontacted to examine the temporal stability of handedness patterns. The Time 2 subsample included 53 participants who scored at least 2 S.D. above the mean on any of the schizotypy dimensions from the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995) or on the Community Assessment of Psychotic Experiences (CAPE; Stefanis et al., 2002) and 76 participants whose scores were less than 0.5 S.D. above the mean on all of these measures. The reassessed participants did not differ from the total sample on sex ($\chi 2(1)=0.69$) or age ($t(849)=1.82$).

2.2. Measures

2.2.1. Psychosis-proneness

Participants completed measures assessing schizotypy and psychotic-like experiences at the initial assessment. The O-LIFE is a widely used questionnaire that contains self-administered subscales assessing schizotypy traits: Unusual Experiences (UnEx), Cognitive Disorganization (CogDis), and Introvertive Anhedonia (IntAn), related to positive, disorganized and negative schizotypy, respectively. This questionnaire has shown an excellent reliability (Burch et al., 1998) and good validity (Startup, 1999). Note that the O-LIFE Impulsive-Nonconformity subscale was not used in the present study. Psychotic-like experiences were assessed with the Spanish version of the CAPE (Ros-Morente et al., 2011), a self-administered instrument including Positive (CAPEPos) and Negative (CAPENeg) symptom subscales. It has good validity and reliability (Konings et al., 2006 and Brenner et al., 2007) and has been used in general (Pfeifer et al., 2009) and adolescent (Yung et al., 2009) population studies. Note that the CAPE Depressive symptom subscale was not included.

2.2.2. Handedness

Handedness was assessed with the 12-item self-report Annett Hand Preference Questionnaire (Annett, 1970) at both assessments. It inquires about hand preference for six primary and six non-primary actions (Table 6); answers are “right”, “either”, and “left”. Following Shaw et al. (2001), subjects were grouped according to the following handedness criteria:

(a) Writing hand. Six hundred and fifty-one right-handed and 65 left-handed subjects were compared. Note that 12 subjects classified “either” were excluded for this comparison.

(b) 3-Way classification. Following Annett (1985), the seven original groups (see next paragraph) were reduced to three: “strong right” (group 1), “mixed” (groups 2–7) and “strong left” (group 8).

(c) 7-Way classification. Subjects were assigned to one of the seven groups: group 1 is Right-pure; group 2, Right-weak Left; group 3, Right-mild Left; group 4, Right-moderate Left; group 6, Left-strong Right; group 7, Left-weak Right; and group 8, Left-pure. Consistent with previous research in this area (e.g. Claridge et al., 1998, Shaw et al., 2001 and Annett and Moran, 2006), we follow Annett's (1985) scoring revision with the original group 5 (Right-strong Left) being re-classified into either three or four, maintaining the original numbering of the remaining groups.

(d) Degree of “ambiguous handedness”. The number of items to which a subject responded to use “either” hand.

(e) Inconsistency across time (Time 2 subsample only). Number of handedness items answered inconsistently across the two assessments. Following Hayden et al. (1997), subjects reporting three or more inconsistent items had “inconsistent hand preference” and subjects with two or fewer inconsistent answers had “consistent hand preference”.

Table 1. Mean scores and S.D. for the selected O-LIFE and CAPE subscales.

	Total (*N*=728)	Female (*n*=364)	Male (*n*=364)	*t* (d.f.=726)	Cohen's *d*
O-LIFE					
UnEx	11.5 (5.9)	12.1 (6.0)	11.0 (5.8)	2.53□□	0.19
CogDis	12.9 (5.0)	13.8 (4.7)	11.9 (5.1)	5.25□□□	0.39
IntAn	6.9 (3.0)	6.3 (2.6)	7.5 (3.2)	−5.72□□□	0.42
CAPE					
CAPEPos	29.9 (6.7)	30.0 (6.9)	29.8 (6.6)	0.23	0.02
CAPENeg	24.3 (5.0)	24.1 (4.8)	24.4 (5.2)	0.61	0.05

A Cohen's *d* value of 0.20 represents a small effect size, 0.50 represents a medium effect size and 0.80 represents a large effect size.*Abbreviations*: UnEx, Unusual Experiences subscale; CogDis, Cognitive Disorganization subscale; IntAn, Introvertive Anhedonia subscale; CAPEPos, CAPE

positive subscale; CAPENeg, CAPE negative subscale.Level of significance: □P≤0.05, □□P≤0.01, □□□P≤0.001.

Table 2. Correlations between selected O-LIFE and CAPE subscales for the total sample (*N*=728) and the re-assessed subsample (*n*=129).

N=728	CogDis	IntAn	CAPEPos	CAPENeg
n=129				
UnEx	+0.47□□□	−0.02	+0.70□□□	+0.39□□□
	+0.56□□□	+0.07	+0.79□□□	+0.46□□□
	CogDis	+0.16□□□	+0.39□□□	+0.51□□□
		+0.36□□□	+0.58□□□	+0.64□□□
		IntAn	+0.06	+0.28□□□
			+0.06	+0.40□□□
			CAPEPos	+0.52□□□
				+0.59□□□

Abbreviations: UnEx, Unusual Experiences subscale; CogDis, Cognitive Disorganization subscale; IntAn, Introvertive Anhedonia subscale; CAPEPos, CAPE positive subscale; CAPENeg, CAPE negative subscale.Level of significance: □P≤0.05, □□P≤0.01, □□□P≤0.001.

Table 3. Mean scores and S.D. for the selected O-LIFE and CAPE subscales by writing hand (*n*=716).

	Left (*n*=65)	Right (*n*=651)	*t* (d.f.=714)	Cohen's *d*
O-LIFE				
UnEx	11.5 (5.6)	11.5 (6.0)	0.00	0.00
CogDis	13.3 (4.7)	12.8 (5.0)	−0.70	0.05
IntAn	6.9 (2.5)	6.9 (3.0)	0.07	0.01
CAPE				

	Left (*n*=65)	Right (*n*=651)	*t* (d.f.=714)	Cohen's *d*
CAPEPos	29.8 (6.1)	29.9 (6.8)	0.15	0.01
CAPENeg	24.2 (5.1)	24.2 (5.0)	0.09	0.01

A Cohen's *d* value of 0.20 represents a small effect size, 0.50 represents a medium effect size and 0.80 represents a large effect size.*Abbreviations*: UnEx, Unusual Experiences subscale; CogDis, Cognitive Disorganization subscale; IntAn, Introvertive Anhedonia subscale; CAPEPos, CAPE positive subscale; CAPENeg, CAPE negative subscale.*Note*: 12 subjects who answered "either" were excluded from this particular analysis.

Table 4. Mean scores and S.D. for the selected O-LIFE and CAPE subscales by 3-way classification of handedness (*n*=728).

	Strong-Left (*n*=24)	Mixed (*n*=211)	Strong-Right (*n*=493)	*F* value (d.f.=2, 722)
O-LIFE				
UnEx	13.6 (5.9)	12.0 (5.9)	11.2 (5.9)	3.13
CogDis	13.7 (4.4)	13.3 (4.6)	12.7 (5.2)	2.08
IntAn	6.8 (2.4)	7.1 (3.1)	6.8 (3.0)	0.07
CAPE				
CAPEPos	31.0 (6.9)	30.6 (7.4)	29.6 (6.4)	1.99
CAPENeg	24.1 (6.0)	24.6 (5.0)	24.1 (5.0)	0.58

Abbreviations: UnEx, Unusual Experiences subscale; CogDis, Cognitive Disorganization subscale; IntAn, Introvertive Anhedonia subscale; CAPEPos, CAPE positive subscale; CAPENeg, CAPE negative subscale.Level of significance: $P \leq 0.05$.

Table 5. Mean scores and S.D. for the selected O-LIFE and CAPE subscales by Annett 7-way classification of handedness.

	Group 1 (*n*=493)	Group 2 (*n*=79)	Group 3 (*n*=67)	Group 4 (*n*=19)	Group 6 (*n*=30)	Group 7 (*n*=16)	Group 8 (*n*=24)	*F* (d.f.=6, 714)	Significant comparisons
O-LIFE									
UnEx	11.2 (5.9)	11.8 (5.6)	13.2 (6.4)	12.4 (6.8)	10.3 (4.6)	10.6 (5.7)	13.6 (5.9)	2.22□	
CogDis	12.7 (5.2)	12.9 (4.3)	13.7 (4.8)	13.7 (4.8)	14.0 (4.4)	11.6 (5.2)	13.7 (4.4)	1.61	
IntAn	6.8 (3.0)	6.5 (3.0)	7.1 (2.9)	8.4 (3.2)	7.0 (1.9)	7.9 (4.8)	6.8 (2.4)	1.48	
CAPE									
CAPE Pos	29.6 (6.4)	29.1 (5.3)	32.3 (8.9)	34.6 (10.5)	29.0 (5.5)	28.8 (5.4)	31.0 (6.9)	4.25□□□	Group 1<Group 3 Group 1<Group 4
CAPE Neg	24.1 (5.0)	23.7 (4.7)	25.4 (5.5)	25.8 (5.3)	24.2 (4.4)	25.3 (5.3)	24.1 (6.0)	0.97	Group 2<Group 4

Group 1: Right-pure; Group 2: Right-weak Left; Group 3: Right-mild Left; Group 4: Right-moderate Left; Group 6: Left-strong Right; Group 7: Left-weak Right; Group 8: Left-pure.*Abbreviations*: UnEx, Unusual Experiences subscale; CogDis, Cognitive Disorganization subscale; IntAn, Introvertive Anhedonia subscale; CAPEPos, CAPE positive subscale; CAPENeg, CAPE negative subscale.Level of significance: □P≤0.05, □□P≤0.01, □□□P≤0.01.

Table 6. Percentage of sample endorsing “either” to each Annett item (except writing hand), ordered from low to high. Alongside are the mean UnEx and CAPEPos scores of the subjects endorsing “either” to the corresponding item considered as a group.

Item	Subjects endorsing “either” *n* (%)	O-LIFE UnEx mean score	CAPE CAPEPos mean score
Hammering (P)	29 (4.0)	13.5	32.7
Scissors	30 (4.1)	13.0	24.9
Throwing ball (P)	38 (5.2)	12.9	31.5
Wielding racket (P)	46 (6.3)	11.9	29.6

Item	Subjects endorsing “either” *n* (%)	O-LIFE UnEx mean score	CAPE CAPEPos mean score
Striking match (P)	60 (8.2)	12.7	30.7
Threading needle	66 (9.1)	12.7	31.1
Brushing teeth (P)	8 (11.1)	12.1	31.2
Dealing cards	87 (12.0)	12.1	30.9
Shoveling	129 (17.7)	11.9	30.2
Sweeping	155 (21.3)	12.0	29.8
Unscrewing jar	157 (21.6)	12.2	30.6

Abbreviations: UnEx, Unusual Experiences subscale; CAPEPos, CAPE positive subscale; (P), primary action.Total number of items=11; UnEx: $r=-0.69$, $P=0.02$; CAPEPos: $r=+0.09$, $P=0.80$.

2.3. Hypotheses

Based upon the literature, we hypothesized the following associations of handedness with psychosis-proneness. We expected the strongest associations of handedness to be with positive schizotypy, consistent with the majority of the previous findings.

(1) Given that the literature supports an association of mixed, rather than pure left, handedness with psychosis-proneness, we expected no differences between left- and right-handed writers.

(2) We expected mixed handed participants to have higher psychosis-proneness scores in comparison to both left- and right-handed participants, and the left-handed participants to score higher than the right-handed participants.

(3) We expected that the 7-way classification of handedness would corroborate the association of mixed handedness, followed by left, handedness, with psychosis-proneness.

(4) We expected highly psychosis-prone subjects to display a higher degree of ambiguous handedness (i.e., using different hands for the same action, following Shaw et al., 2001).

(5) We predicted the effect of mixed handedness for psychosis-proneness would be more evident for subjects with ambiguous handedness (any “either” score) than for subjects with non-ambiguous handedness.

(6) We hypothesized that subjects with inconsistent hand preference across the two assessments would score higher on ratings of psychosis-proneness and psychotic-like experiences.

2.4. Statistical analyses

A series of analyses of variance (ANOVAs) were performed to examine the main effects of handedness, sex, and their interaction on the O-LIFE and CAPE subscales. If appropriate, post-hoc comparisons with Tukey's Honestly Significant Difference (HSD) test were applied. For the analysis of “either” score, bivariate Pearson correlation was used. All significant values are two-tailed and relied on a $P<0.05$ threshold to evaluate statistically significant differences or associations.

3. Results

Scores on the psychosis-proneness scales ranged from −1.3 S.D. to +4.9 S.D., indicating a wide range of variability on these constructs in the sample. Females had significantly higher scores on UnEx and CogDis, whereas males scored significantly higher on IntAn. No significant sex differences were found for the CAPE (Table 1). The correlations of the psychosis-proneness scales for the total sample and the Time 2 subsample were comparable (Table 2).

3.1. Classification by writing hand

As hypothesized, participants identified as right-handed or left-handed based upon writing hand did not differ on the O-LIFE or CAPE (Table 3). There were no significant writing hand×sex interactions.

3.2. Three-way classification of handedness

The three groups differed significantly on UnEx, although post-hoc tests showed no significant differences between groups (Table 4). No significant differences resulted for the other O-LIFE subscales, CAPE, or the sex×handedness interactions.

3.3. Seven-way classification of handedness

Significant effects of the 7-way classification were found for UnEx and for CAPEPos (Table 5). None of the post-hoc comparisons were significant for the UnEx scores. On the CAPEPos, handedness group 1 scored significantly lower than groups 3 ($P=0.03$) and 4 ($P=0.02$), and group 4 also scored significantly higher than group 2 ($P=0.02$). The handedness×sex interactions were not significant.

3.4. Ambiguous handedness

The Pearson correlation of psychosis-proneness measures with the number of items answered either hand preference was significant for UnEx ($r_{(726)}$=+0.10, P=0.01), and CAPEPos ($r_{(726)}$=+0.08, P=0.04), although they represent modest effect sizes. These associations were moderated by sex, as females showed significant correlations for both UnEx ($r_{(362)}$=+0.15, P=0.00) and CAPEPos ($r_{(362)}$=+0.11, P=0.03), although results were not significant for males. Thus, highly psychosis-prone females, but not males, were less consistent in hand preference across items.

The percentage of subjects responding "either" to each of the 11 Annett items (excluding writing hand) varied widely (Table 6), indicating that some activities (notably primary actions) rarely involved ambiguous handedness. In order to examine whether psychosis-proneness was more strongly related with ambiguous handedness on such tasks, we calculated the correlation of the percentage of subjects endorsing "either" to each Annett item with their UnEx and CAPEPos scores (following Shaw et al., 2001). As writing hand was analyzed previously, it was not considered for this analysis. As in Shaw et al. (2001), most items answered "either" referred to non-primary actions, and higher UnEx scores were significantly and inversely related to the proportion of subjects using "either hand" for each action ($r_{(9)}$=−0.69, P=0.02). Further exploration showed that again the effect was due to females (UnEx, $r_{(9)}$=−0.72, P=0.01; CAPEPos, $r_{(9)}$=−0.56, P=0.08), as males did not corroborate the association (UnEx, $r_{(9)}$=−0.31; CAPEPos, $r_{(9)}$=−0.01). In other words, females using either hand for actions that few other people endorsed showed higher UnEx scores than subjects using either hand for actions more commonly performed with either hand. Thus, the association between higher UnEx scores and the "either" handedness item appeared evident in female subjects who responded "either" to less commonly ambiguous primary actions.

3.5. Further analysis of mixed- vs. ambiguous-handedness

Following Shaw et al. (2001), we examined whether there was an additive effect of the ambiguous-handedness (number of actions for which "either hand" is used) and the standard scoring of mixed-handedness (using the right hand consistently for some actions and the left hand for others). To this end, the sample was subdivided based upon whether participants gave any "either" answer on the Annett scale. The resulting "zero either score" (not ambiguous) and "any either score" (ambiguous) groups were balanced (46.8% and 53.2% of the sample, respectively). We examined the effects of the 3-way and the 7-way classifications independently for the "zero either score" and the "any either score" groups. For the "zero either score" group, the 3-way classification had a significant effect for UnEx, and the 7-way classification differed significantly for CAPEPos. For the "any either score" group, the 7-way classification was significant for IntAn and CAPEPos (Table 7). It is important to note that the sample size of the Right-moderate Left group was small and thus requires replication.

Table 7. Data divided according to “either” score on the Annett scale.

(a) Subjects with “zero either score” (not ambiguous) (*n*=341)							
Annett 3-way classification							
UnEx	Strong right (*n*=234)		Mixed (*n*=89)		Strong left (*n*=18)		
Mean (S.D.)	10.7 (6.0)		11.2 (5.5)		14.7 (5.7)		
$F_{(2,338)}$=3.82, *P*=0.023							
Post-hoc contrasts:	Strong right<Strong left; *P*=0.017						
Annett 7-way classification							
CAPEPos	Group 1 (*n*=234)	Group 2 (*n*=36)	Group 3 (*n*=28)	Group 4 (*n*=13)	Group 6 (*n*=9)	Group 7 (*n*=3)	Group 8 (*n*=18)
Mean(S.D.)	29.3 (6.6)	27.7 (4.6)	32.5 (8.9)	32.3 (7.9)	28.0 (4.0)	24.3 (5.9)	32.4 (7.1)
$F_{(6,334)}$= 2.76, *P*=0.012							
Post-hoc contrasts:	Not significant						
(b) Subjects with “any either score” (ambiguous) (*n*=387)							
Annett 7-way classification							
IntAn	Group 1 (*n*=259)	Group 2 (*n*=43)	Group 3 (*n*=39)	Group 4 (*n*=6)	Group 6 (*n*=21)	Group 7 (*n*=13)	Group 8 (*n*=8)
Mean (S.D.)	6.8 (3.0)	6.2 (2.6)	7.0 (3.0)	10.2 (3.2)	7.2 (2.0)	8.2 (5.4)	8.7 (2.2)
$F_{(6,380)}$=2.38, *P*=0.029							
Post-hoc contrasts:	Group 2<Group 4; *P*=0.041						

CAPEPos	Group 1 (*n*=259)	Group 2 (*n*=43)	Group 3 (*n*=39)	Group 4 (*n*=6)	Group 6 (*n*=21)	Group 7 (*n*=13)	Group 8 (*n*=8)
Mean (S.D.)	29.8 (6.3)	30.2 (5.6)	32.1 (9.1)	39.5 (14.2)	29.5 (6.0)	29.9 (5.0)	26.7 (3.9)
$F_{(6,380)}$=2.84, *P*=0.012							
Post-hoc contrasts:		Group 1<Group 4; *P*=0.008		Group 7<Group 4; *P*=0.051			
		Group 2<Group 4; *P*=0.024		Group 8<Group 4; *P*=0.015			
		Group 6<Group 4; *P*=0.020					

Group 1: Right-pure; Group 2: Right-weak Left; Group 3: Right-mild Left; Group 4: Right-moderate Left; Group 6: Left-strong Right; Group 7: Left-weak Right; Group 8: Left-pure.*Abbreviations*: UnEx, Unusual Experiences subscale; IntAn, Introvertive Anhedonia subscale; CAPEPos, CAPE positive subscale.

3.6. Hand preference inconsistency across time

Ninety-four of the 129 re-assessed participants at Time 2 were classified as having a “consistent hand preference” across the assessments. The consistent and inconsistent subjects did not differ significantly, although trends were observed for UnEx and CAPEPos (Table 8). The interactions of inconsistent hand preference and sex were not significant.

Table 8. Mean scores and S.D. for the selected O-LIFE and CAPE subscales by hand preference inconsistency across time (*n*=129).

	Inconsistent (*n*=35)	Consistent (*n*=94)	*t* (d.f.=127)	Cohen's *d*
O-LIFE				
UnEx	12.4 (7.6)	10.7 (5.9)	−1.40	0.25
CogDis	13.1 (5.8)	12.1 (5.1)	−0.95	0.17
IntAn	7.3 (3.9)	7.1 (3.5)	−0.29	0.05
CAPE				

	Inconsistent (*n*=35)	Consistent (*n*=94)	*t* (d.f.=127)	Cohen's *d*
CAPEPos	32.1 (9.2)	29.6 (7.1)	−1.67	0.30
CAPENeg	25.5 (6.7)	24.2 (6.0)	−1.10	0.20

A Cohen's *d* value of 0.20 represents a small effect size, 0.50 represents a medium effect size and 0.80 represents a large effect size.*Abbreviations*: UnEx, Unusual Experiences subscale; CogDis, Cognitive Disorganization subscale; IntAn, Introvertive Anhedonia subscale; CAPEPos, CAPE positive subscale; CAPENeg, CAPE negative subscale.

4. Discussion

Overall results lend partial support to the notion that a shift away from pure dextrality is related to psychosis-proneness. Some of our findings are consistent with previously reported studies on the association of handedness with psychosis-proneness in nonclinical samples (e.g., Somers et al., 2009, Chapman et al., 2011 and Hori et al., 2012). Corroborating previous findings (Shaw et al., 2001, Gregory et al., 2003 and Annett and Moran, 2006), writing hand alone was not associated with psychosis-proneness. Annett's 7- and 3-way classifications showed that left-handers did not differ significantly from other groups. Contrary to previous findings (Annett and Moran, 2006 and Shaw et al., 2001), the pure left-handed group did not differ from the mixed- or right-handed groups. In our study, Annett's 7-way right-handers with strong/moderate left tendencies (i.e., mixed handed) were more psychosis-prone than pure right-handed subjects. These findings can be interpreted as being consistent with the hypothesized role of disrupted lateralization in the etiology of schizophrenia (e.g., Crow, 1990, Sommer et al., 2001, Schiffman et al., 2005 and Oertel et al., 2010) and as a genetic risk marker for the disorder (e.g., Altamura et al., 2012).

Ambiguous handedness was associated with psychosis-proneness, particularly for females on the positive dimension at trait and symptom-like levels. Sex differences in hemispheric lateralization are well documented, showing the atypical pattern of left-handedness being more common in males. Unusual cases of females with atypical handedness, with an even more unusual pattern of ambiguous handedness, might evidence particular brain lateralization disturbances highly associated to psychosis proneness. Moreover, as in the study by Shaw et al. (2001), this association appeared particularly dependent on subjects who used “either” hand for less commonly ambiguous actions. Similarly, Annett and Moran (2006) found that the highest schizotypy scores corresponded to right-handed writers who perform other primary actions with the left hand. These authors suggested that discordance for primary actions is not a general risk for both right- and left-handed writers, but only for the former, suggesting that the classification

of mixed-handedness should be further refined to examine the specific subgroup of right-handed writers who perform other primary actions with the left hand.

Not only did these findings confirm the hypothesis that the effect of mixed handedness for psychosis-proneness is more evident for subjects with ambiguous handedness than for subjects with non-ambiguous handedness, but we found that left-handedness had a significant effect on the latter. Consistent with Shaw et al. (2001), we found significant differences on UnEx scores for the non-ambiguous group. On the other hand, the ambiguous group showed differences on IntAn and CAPEPos scores. Therefore, when we observe subjects exclusively using one hand for a specific action (non-ambiguous), left-handers (not mixed) are significantly more psychosis prone than right-handers. On the other hand, when observing ambiguous-handers, the most mixed group (right with strong left tendency) scored significantly higher than both left- and right-handers. Furthermore, the effect of left-handedness on non-ambiguous groups was evident for positive schizotypy, whereas the effect of mixed-handedness on ambiguous groups was evident for negative schizotypy and positive symptom dimension. Note that this is only the second study, after Shaw et al. (2001), to perform these analyses; therefore, replication is needed. A reserved interpretation of these results would align with the idea of a prenatal hemispheric insult as origin of hand dominance, and being bilateral and diffuse, it is unlikely to induce a complete change in hand dominance (Dragovic et al. 2005); thus, left-handers would show higher psychosis proneness than right-handers when ambiguous handedness is present for all.

We also considered hand-preference inconsistency across time as a measure of atypical handedness as proposed by Hayden et al. (1997). Although the inconsistent group scored higher than the consistent group on every scale on visual inspection, only a trend for significant differences was found.

Although the effects were generally small, we tended to find a stronger association of atypical handedness with the positive dimension of schizotypy/psychosis proneness than with the negative dimension. Nevertheless, other indicators of neurodevelopmental impairment, such as developmental instability have stronger associations with negative schizotypy (Rosa et al., 2000, Barrantes-Vidal et al., 2003 and Kaczorowski et al., 2009). Prenatal indicators of developmental disturbances occurring in a narrow prenatal time window, such as dermatoglyphic anomalies, might relate to negative schizotypy, resembling the pattern found in schizophrenia (Rosa et al., 2000), whereas later functional lateralization, reflected by handedness, might be more related to positive schizotypy.

This study indicated that both trait and symptom-like measures of positive psychosis-proneness are associated with patterns of atypical handedness. Although some psychosis-proneness instruments were originally designed for older adolescents and adults, they can be reliably applied to adolescents to estimate the expression of nonclinical symptom-oriented (Wigman et al., 2011 and Yung et al., 2009) and trait-oriented (Barrantes-Vidal et al., 2003 and Alvarez-Moya et al., 2007) psychosis vulnerability. Also, adolescent samples allow the study of nonclinical characteristics before the typical age of onset of frank psychotic symptoms in later adolescence or early adulthood (Tandon et al., 2008).

In summary, this study shows that both schizotypy traits and nonclinical psychotic-like experiences are present and can be assessed in adolescents and offers partial support to their association with atypical handedness. Results partially support mixed-handedness as a reliable marker of developmental disorders underlying both atypical lateralization and psychosis-proneness. Among various possible mixed-handedness patterns, inconsistent hand use across primary actions and within the same action across time seems to be particularly related to psychosis-proneness.

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